PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference P6004169PCT	FOR FURTHER ACTION	See Form PCT/IPEA/416
International application No. PCT/NL2004/000106	International filing date *(day/month/year)* 12.02.2004	Priority date *(day/month/year)* 12.02.2004

International Patent Classification (IPC) or national classification and IPC
INV. A61K38/01 A61K38/02 A61P3/00 A61P9/00 A61P3/10 A61P9/12 A61P17/00

Applicant
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1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 7 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☐ *sent to the applicant and to the International Bureau)* a total of sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in celectronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☐	Box No. II	Priority
☒	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
12.12.2005	12.06.2006

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INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/NL2004/000106

Box No. I Basis of the report

1. With regard to the language, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
   - ☐ international search (under Rules 12.3 and 23.1(b))
   - ☐ publication of the international application (under Rule 12.4)
   - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the elements* of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

Description, Pages	
1-20	as originally filed

Claims, Numbers	
1-28	as originally filed

   ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☒ The amendments have resulted in the cancellation of:
   - ☐ the description, pages
   - ☒ the claims, Nos. 15-28
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/NL2004/000106

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 1-14(all partially)

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (specify):

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos. 1-14 (all partially) (see separate sheet)

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	☐	has not been furnished
	☐	does not comply with the standard
the computer readable form	☐	has not been furnished
	☐	does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/NL2004/000106

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-14
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-14
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-14
	No:	Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

Re Item III.

1. Claims 1-14 relate to a product/compound defined by reference to a desirable characteristic or property, namely "..mixture of peptides, the peptides comprising at least 6.5 % wt cysteine". The claims cover all products/compounds/ having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such products/compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. An attempt is made to define the product /compound by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Moreover, claims 2,5,11 relate to the treatment of diseases which are functionally defined or which do not fall within the definition of a disease ("reducing effects of alcohol consumption", "boosting vitality", and "treating drug-induced toxicity"), (e.g. the applicant's attention is drawn to the fact that "effects of alcohol consumption" as such cannot generally be considered as a diseases to be treated. For instance reasonable consumption of red wine is reported to reduce atherosclerosis and associated cardiovascular diseases). The claims thus cover a rather large number of conditions, whereas the application provides support within the meaning of Article 6 PCT and disclosure within the meaning of Article 5 PCT for only a very limited number of conditions. In the present case, the claims so lack support and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims 2,5,11 also lack clarity because it is not fully possible to determine the diseases for which protection might legitimately be sought (Article 6 PCT).

Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the use of cysteine rich or cysteine containing peptides/mixtures for the treatment of conditions as in claims 4,6-10,12,13; and with due respect to the general idea of the invention.

No opinion will be given in respect of subject matter which is not covered by the search report (Rule 66.1(e)PCT)

Re Item V.

The following documents are referred to in this communication:
D1: EP-A-0 655 244
D2: US-A-4 496 548
D3: US 2003/087819 A1
D4: EP-A-0 787 741

1 NOVELTY (Art. 33(2) PCT)

1.1 The present application appears to meet the requirements of Article 33(2) PCT, because the subject-matter of claims 1-14, insofar as clear, is not new in respect of the prior art as defined in the regulations (Rule 64(1)-(3) PCT):

1. Document D1 discloses the use of a composition of cysteine rich peptides or hydrolysates thereof containing 3% or more cysteine (the use preferably 3-10% cysteine is mentioned in generic terms) for the therapy of conditions associated with infection (metabolic dysfunctions, diabetes, inflammation, CVD (tachycardia). D1 does not disclose the use of a mixture of cysteine rich of the present application for restoring thiol homeostasis and the therapy of associated conditions (see passages cited in the search report).

2. Document D2 discloses the use of a composition which may contain 10-90% by weight of a compound selected from cysteine and cysteic acid in a mixture further containing thiamine, ascorbic acid and a flavonoid for the treatment of hangover and fatigue associated with alcohol consumption (see passages cited in the search report). D2 concerns the amino acid cysteine as such but it does not disclose the use of the compositions of the present invention for restoring thiol homeostasis and the therapy of associated conditions (see passages cited in the search report).

3. Document D3 discloses the use of cysteine-containing peptides (ApoA-1 Milano/Paris) for therapy of cardiovascular diseases. The specifically disclosed peptides are 18'mers containing one cysteine residue (5.6 wt%). The use of a mixture of cysteine rich of the present application for restoring thiol homeostasis is not mentioned (see passages cited in the search report).

4. Document D4 discloses a cysteine rich peptide for therapy of type II diabetes (NIDDM). The peptide disclosed is 37 amino acid in length with two cysteine residues in the N-terminal portion, resulting in 5.2 wt% cysteine. The use of a mixture of cysteine rich of the present application for restoring thiol homeostasis is not mentioned (see passages cited in the search report)

Therefore, the subject matter of claims 1-14 appears new (Article 33(2) PCT).

2 INVENTIVE STEP (Article 33(3) PCT)

2.1 Although it is well known in the art that thiol group containing peptides such as glutathione (tripeptide: gamma-glutamylcysteinylglycine) are involved in thiol homeostasis, the prior does not suggest that a mixture of cysteine rich peptides obtained by hydrolysis and fractionation of whey proteins is effective in restoring thiol homeostasis and the treatment of diseases associated with an imbalance of thiol homeostasis.

Therefore, the subject-matter of the claims 1-14 appears to involve an inventive step in the sense of Art. 33(3) PCT.

3 INDUSTRIAL APPLICABILITY (Article 33(4) PCT)

3.1 Claims 1-14, insofar as clear, fulfil the requirements of (Article 33(4) PCT).